Progressive Increases in the Amplitudes of the Maxima and Minima in the Systolic and Diastolic Times of the First Derivative of the Arterial Pulse Wave Morphology in Response to Incremental Exercise

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Abstract

The present study aimed to assess the effects induced by continuous and linearly increased to maximum isometric exercise (LIMIE) on time courses of: amplitudes of the maximum (SA_{max}) and minimum (SA_{min}) in the systolic time (ST) and the maximum (DA_{max}) and minimum (DA_{min}) in the diastolic time (DT) and of interval period (IP), ST and DT. This set of features was chosen for quantitatively characterizing the entire arterial pressure wave first derivative (APWFD) morphology. LIMIE provoked progressive growing in the time courses responses of: Increments of SA_{max}, SA_{min}, DA_{max}, and DA_{min}, moderately correlated with the increments of the muscular force. The time courses of SA_{max} and SA_{min} were similar, DA_{max} greater than DA_{min}, SA_{max} and SA_{min} greater than DA_{max} and DA_{min}, supported by the equality or inequality of regression slopes and the difference between mean values of baseline to maximum (D_{BMax}). Shortening, proportional, and greater of IP with DT than ST, supported by the greater correlations and D_{BMax}. Our findings show that LIMIE induces simultaneous gradual increments in the y-axis and shortenings in the x-axis in the entire APWFD morphology. Changes characterized quantitatively by the gradual increments of SA_{max}, SA_{min}, DA_{max}, and DA_{min} and shortenings of IP, DT, and ST, a set of features that are simple, visually noteworthy, and easily extractable.

1. Introduction

The amplitudes of maxima and minima and the periods between zero crossings can be considered as visually noteworthy and easy to extract features of the arterial pulse waveform (APW) first derivative (APWFD) morphology. The study of these features has focused exclusively on the first maximum of APWFD morphology, the arterial dP/dt_{max}. This measure is considered a consistent indicator for the overall assessment of left ventricular (LV)-arterial function, specifically contractility and its degree of deterioration caused by cardiovascular disease [1], especially in heart failure [2] and shock patients. Additionally, maxima, minima, and intervals between zero crossings are used in photoplethysmographic pulse wave analysis (PPG-PWA) studies as a means for accurately detecting relevant features of APW, such as pulse onset, systolic peak, dicrotic notch, and diastolic peak [3]. The maxima, minima, and periods between zero crossings represent a small subset of the numerous features extracted from the APWFD used for assessing arterial stiffness, blood pressure, and cardiovascular aging [4].

The performance of isometric exercise (IE) induces cardioacceleration and pressor responses, mediated by an upsurge in sympathetic activity, reinforced by the activation of the metaboreflex (MBR) [5]. These effects are attenuated in patients with heart failure [5] and exaggerated in patients with metabolic syndrome [6].

We hypothesize that the features — maxima, minima, and time between zero crossings — of the APWFD morphology respond jointly, dynamically, and distinctly to maneuvers that induce changes in cardiovascular function. Specifically, the generation of progressive, convincing changes in the amplitudes of maxima, minima, and periods caused by an IE maneuver of linearly increased to the maximum muscular force (LIMIE), which produces gradual increases in blood pressure and heart rate (HR). To test this assumption, we assessed and compared in healthy volunteers the effects of performing LIMIE on the time courses of the amplitudes of the maximum (SA_{max}) and minimum (SA_{min}) during the systolic time (ST), the maximum (DA_{max}) and minimum (DA_{min}) during the diastolic time (DT), the duration of the interbeat period (IP), and of its subperiods ST and DT, all features extracted from the APWFD morphology.

2. Methods

2.1. Subjects

Thirty-one young, healthy, non-smoking, and sedentary volunteers participated, 20 men and 11 women. Their age, height, and weight were 23.4±2.5 years, 165±4 cm, and

64.2±12.0 kg, respectively. Written informed consent was requested for participation. The ethics committee of our university approved this study.

2.2. Protocol

During the first visit to the laboratory, the subjects' health status was evaluated, and they were trained to execute LIMIE correctly. In the second visit, subjects performed static leg extension (LE) while sitting. Each session consisted of three successive stages: 1 minute of control, incremental isometric right LE at a rate of 0.21 $kg \cdot s^{-1}$ until exhaustion, where the maximum muscular force (MF) is attained, and a 2-minute recovery period. The subjects' MF signal was displayed on a screen so that they could follow a linear pattern.

2.3. Signal recording and acquisition

ECG was detected at the thoracic bipolar lead CM5 and a bioelectric amplifier (Biopac Systems). APW was recorded by Finapres (Ohmeda). The MF signal was recorded from a handgrip dynamometer (Stoelting), attached to a chair to measure MF during isometric LE. All signals were digitized at a sampling rate of 1 kHz via an acquisition and display system (Biopac Systems).

2.4. Data processing

The set of features extracted in a beat-to-beat format from the APWFD was: the maximal (A_{max}) and minimal (A_{min}) amplitudes contained in the IP, computed as the period between successive onsets, marked by the first zero crossing of each beat. IP was divided into ST, the time lapse from the first to the third zero crossing, and DT, the time from the third zero crossing to the next onset. A_{max} and A_{min} were classified into those contained in ST (SA_{max} and SA_{min}) and those contained in DT (DA_{max} and DA_{min}).

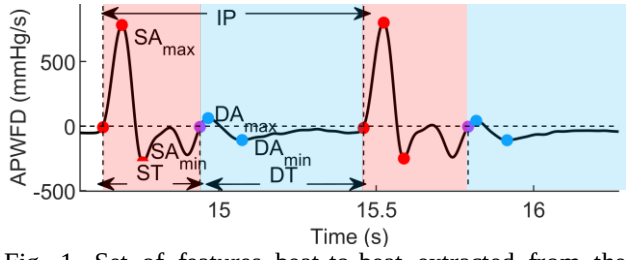

Fig. 1. Set of features beat-to-beat extracted from the APWFD signal, SA_{max} and SA_{min}, contained in ST, and DA_{max} and DA_{min} contained in DT.

These features were used to form the time series, which were cubic-spline interpolated and resampled at 4 Hz. MF was normalized for the individual maximal force and expressed as a percentage ($\%MF_{max}$). The characterization of the response of the APWFD features to LIMIE was carried out by the computation of the ensemble averages of the time courses to highlight any response pattern, by the construction of the continuous relationships between the APWFD features vs. $\%MF_{max}$, and by comparing the time courses of the indices through correlations, regression slopes (RSL), and the difference between the values of each feature at baseline and at 100%MF_{max} (D_{BMax}) to evaluate the maximum effect.

2.5. Statistical Analysis

Data is expressed as mean±SD. Correlations and linear regressions of the time courses of the features vs. $\%MF_{max}$ and the D_{BMax} were calculated for each subject. ANOVA for repeated measures was employed to compare the correlations, RSL, and D_{BMax} between features. Post-hoc pairwise comparisons were performed by the Tukey test. Statistical significance was accepted at $p<0.05$.

3. Results

In LIMIE, MF showed a mean correlation of 0.998±0.001 vs. time and induced, in a beat-to-beat format: 1) proportional increases in SA_{max}, SA_{min}, DA_{max}, and DA_{min} in relation to $\%MF_{max}$. These features showed moderated mean correlations with $\%MF_{max}$ (Fig. 2).

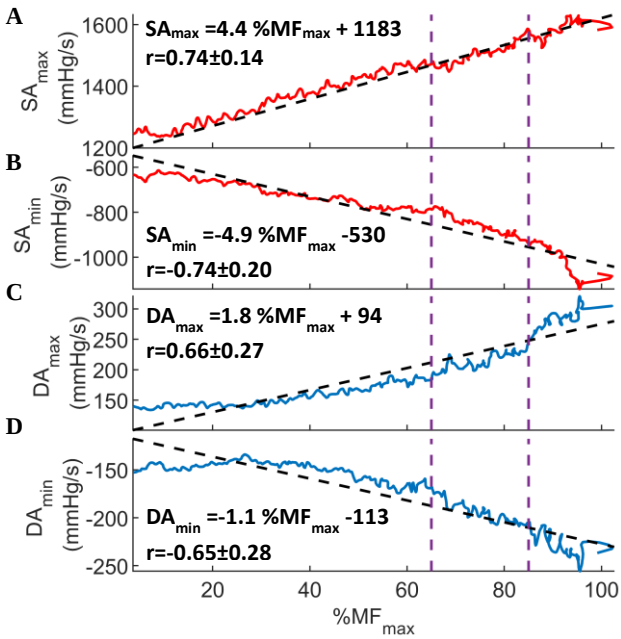

Fig. 2. Ensemble averages and the respective correlations and linear regressions of $\%MF_{max}$ vs. A) SA_{max}, B) SA_{min}, C) DA_{max}, D) DA_{min} during LIMIE.

Both mean RSL and mean D_{BMax} were similar in SA_{max} and SA_{min}, greater in DA_{max} than in DA_{min}, and greater ($p<0.001$) in SA_{max} and SA_{min} than in DA_{max} and DA_{min} (Fig. 2, Table 1).

Table 1. Mean±SD of A_{max} and A_{min} in ST and DT of APWFD at 0 (control), at 100 $\%MF_{max}$, and their respective D_{BMax} (N=31).

	SA_{max} (mmHg/s)	SA_{min} (mmHg/s)	DA_{max} (mmHg/s)	DA_{min} (mmHg/s)
0 $\%MF_{max}$	1264±319	-640±250	138±47	-148±27
100 $\%MF_{max}$	1757±477	-1131±489	323±213	-273±179
D_{BMax}	493±305†	506±398†	155±149*	123±173*†

* $p<0.008$ vs. D_{BMax} of SA_{max}
†$p<0.05$ vs. D_{BMax} of DA_{max}

2) Proportional shortening in IP, DT and ST with respect to $\%MF_{max}$. The mean correlations with $\%MF_{max}$ were strong for IP and DT, and weak for ST (Fig. 3). Both the mean RSL and D_{BMax} of DT and IP were similar, and those of ST were smaller ($p<0.001$) (Fig. 3, Table 2).

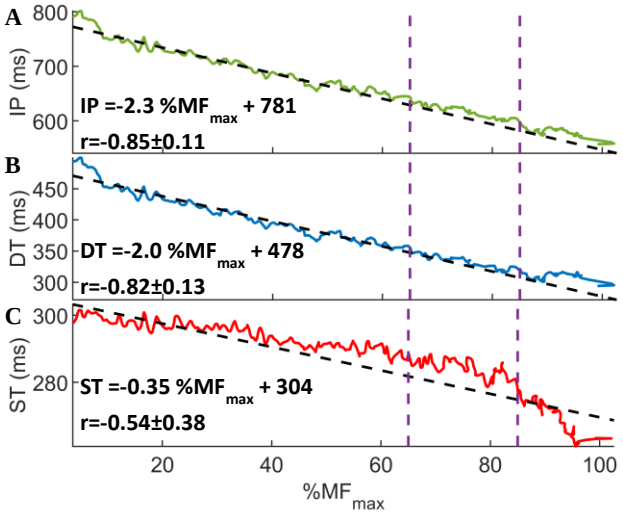

Fig. 3. Ensemble averages and linear regressions and correlations of $\%MF_{max}$ vs. A) IP, B) DT, C) ST.

Table 2. Mean±SD IP, ST, and DT at 0 (control) and at 100 $\%MF_{max}$ and their respective D_{BMax} (N=31).

	IP (ms)	DT (ms)	ST (ms)
0 $\%MF_{max}$	816±89	518±80	298±19
100 $\%MF_{max}$	527±78	255±59	242±39
D_{BMax}	289±72*	263±69*	56±35

* $p<0.001$ vs. D_{BMax} of ST

The ensemble average of the relationships between $\%MF_{max}$ and SA_{max}, SA_{min}, DA_{max}, and DA_{min} showed, at around $65\%MF_{max}$, the visually detected onset of a greater rate of increment and of shortening in ST, which intensified around $85\%MF_{max}$ (Figs. 2 & 3).

The relationships between the progressive shortening of IP and the progressive increment of SA_{max}, SA_{min}, DA_{max}, and DA_{min}, as well as the progressive shortening of ST and DT, were moderately proportional, as indicated by their respective correlations (Fig. 4).

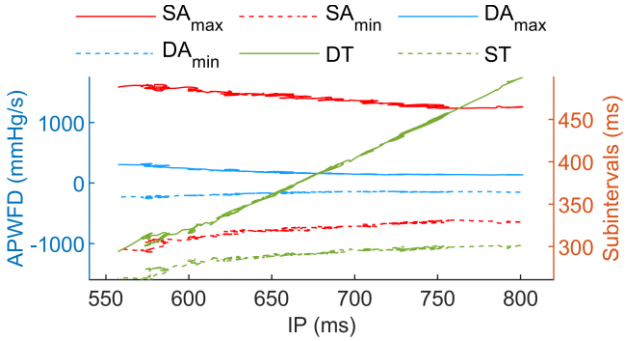

Fig. 4. Ensemble averages and correlations of IP vs. SA_{max}, SA_{min}, DA_{max}, DA_{min}, ST, and DT.

4. Discussion

The main finding of the present study is that LIMIE causes progressive changes in the entire APWFD morphology, characterized, integrated, and quantified by the relationships of IP vs. SA_{max}, SA_{min}, DA_{max}, DA_{min}, DT, and ST. This finding provides relevant knowledge that extends and refines the fields of study of PPG-PWA and the physiology of IE.

The usual IE protocols consist of a single load of low to medium intensity, typically 30% of the maximal voluntary contraction, sustained for five minutes to assess the response in steady-state conditions [7]. In contrast, LIMIE induces progressive, continuous changes in the APWFD features, allowing for the construction of continuous relationships with the $\%MF_{max}$ and the analysis of their time-course responses in non-steady conditions.

The LV-arterial function system, when stimulated by LIMIE, shows a very strong correlation with time, provoking a response in the APWFD features that exhibits ostensibly lower correlations than those of the input (Figs. 2&3). The correlations of the $\%MF_{max}$ vs. features that characterize this system indicate the moderate linearity of its nonstationary performance. Contributing to the lower linearity of the response, the greater abrupt rate increases in SA_{max}, SA_{min}, DA_{max}, DA_{min}, and the greater abrupt shortening in ST, located at around $65\%MF_{max}$ and accentuated at around $85\%MF_{max}$ (Figs. 2&3). Effects possibly caused by the onset of MBR activation, a mechanism that participates in the performance of IE, which, by increasing sympathetic activity, reinforces cardiac and vasomotor functions [5,6].

The APWFD features have been used with two aims:
1. SA_{max} (arterial dP/dt_{max}) has been extensively used as a functional measure, first as an index of LV contractility, and recently, for monitoring the global LV-arterial function [2]. However, very few studies have used the SA_{min} of LV pressure as an LV relaxation rate index, which is reduced in hypertrophic cardiomyopathy [8]. In contrast, for DA_{max} and DA_{min} there are no reports available.
2. As a means to accurately detect numerous APW features, which are systematically employed in the

growing field of PPG-PWA [3].

We found no studies on the effect of IE on AdP/dt_{max}, nor on any provocative maneuver on the entire APWFD morphology, as evaluated by the specific set of features A_{max} and A_{min} in ST and DT.

The present study documents the following specific attributes of the progressively growing response of APWFD fiducial points to LIMIE:

- Progressive increase from 0 to 100%MF_{max} in A_{max} and A_{min} in both ST and DT, supported by their moderate correlations, suggesting that SA_{max} changes drive the proportional changes in SA_{min}, DA_{max} and DA_{min} (Fig. 2).
- Similarity of progressive changes of SA_{max} with SA_{min}, symmetry supported by the similarity of the RSL and of D_{BMax} (Fig. 2, Table 1).
- Greater change in DA_{max} than in DA_{min}, asymmetry documented by the higher RSL and D_{BMax} (Table 1).
- Growing changes of SA_{max}-SA_{min} greater than DA_{max}-DA_{min}, asymmetry supported by the greater RSL and D_{BMax} of the former than the latter (Fig. 2, Table 1).
- Increasing shortening of IP and DT, highly correlated with $\%MF_{max}$, and slight shortening of ST, with low correlation with $\%MF_{max}$ and lower SRL and D_{BMax} (Fig. 3, Table 2), supporting that the progressive IP shortening is at the expense of the progressive DT shortening, with a slight shortening in ST.
- Similarity of the progressive changes of IP and DT, symmetry documented by RSL and D_{BMax} (Fig. 3, Table 2). Difference in the progressive shortenings of DT and ST, documented by the lower RSL, D_{BMax}, and correlations presented by ST (Fig. 3, Table 2).

The joint use of our LIMIE protocol with the time series of A_{max} and A_{min} in ST and DT of the APWFD morphology and their functional attributes mentioned above, all characterized, integrated, and quantified by the relations of IP vs. SA_{max}, SA_{min}, DA_{max}, DA_{min}, ST, and DT (Fig. 4), allows for a dynamic protrayal - analogous to a motion picture - of the response of LV-arterial function to IE, consisting of: progressive beat-to-beat increment of the LV function, modulated by the growing afterload that induces a progressive increase of similar amplitude of the maximal velocities of ascent and descent of pressure in ST (from the opening to the closing of the aortic valve) (Fig. 5).

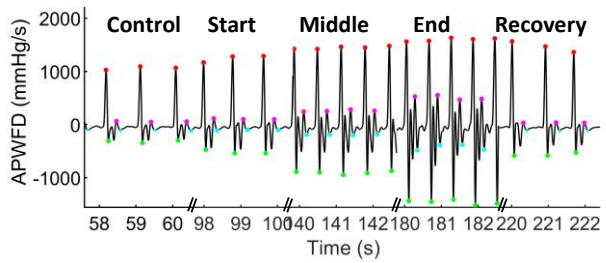

Fig. 5. Representative example of the progressive changes in SA_{max}, SA_{min}, DA_{max}, and DA_{min} during progressively shortened IP at different times of LIMIE.

These changes induce a progressive increase in the Windkessel effect, modulated by the gradual increase in arterial impedance, which provokes a growing rise in the maximal velocities of pressure ascent and descent during DT (from the closing to the opening of the aortic valve) (Fig. 5), with the former being larger than the latter. All this is happening simultaneously at an increasing number of beats per minute, which stems from the progressive shortening of DT and the slight ST reduction.

In conclusion, LIMIE causes gradual changes in the entire APWFD morphology, characterized by a progressive and proportional amplitude increment in the *y*-axis and reductions in the *x*-axis, which are integrated and quantified by the relations of IP vs. SA_{max}, SA_{min}, DA_{max}, DA_{min}, DT, and ST. Hence, the beat-to-beat computation of this set of simple features may enable an integrative analysis of the gradual changes in APWFD morphology resulting from any intervention or cardiovascular disease.

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